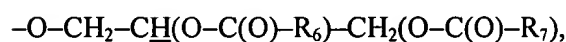


Applicants wish to thank the Examiner for pointing out the obvious error in the formulas describing the branched lipophilic moieties of compounds such as that represented by formula (II) on page 15 of the specification. In the corrected formulas following, the second carbon properly indicates the single hydrogen of the glycerol moiety from which the lipophilic substituents are attached:



Amendments have been made to include inadvertently omitted indications of the positively charged nitrogens of certain of the nitrogen based substituents. This amendment merely clarifies the understood cationic nature of the amino sugar at useful pH, i.e. a pH at which the amino sugar has a cationic nature able to interact with anions such as polynucleotides.

Consistent amendments throughout the specification are respectfully requested as follows:

#### IN THE SPECIFICATION

- NE Not clear
- 1) Please delete the <sup>second</sup> ~~third~~ full paragraph on page <sup>6</sup> ~~5~~, starting from line <sup>17</sup> ~~27~~ and ending with line 10 of page 6 with the following replacement paragraph:

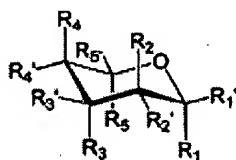
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In a first aspect, the invention features a compound comprising a glycosyl moiety having a nitrogen-based substituent linked to a carbon atom within the glycosyl moiety, where the nitrogen-based substituent is selected from the group

consisting of  $-\text{NH}_2$ ,  $-\text{N}^+(\text{CH}_3)_3$ ,  $-(\text{CH}_2)_n-\text{N}^+(\text{R}_{10})_3$ , and  $-\text{NH}-\text{C}(\text{N}^+\text{H}_2)-\text{NH}_2$ , and where substituents linked to other carbon atoms within the glycosyl moiety are selected from the group consisting of hydrogen,  $-\text{alkyl}$ ,  $-\text{O}-\text{alkyl}$ ,  $-\text{O}-\text{C}(\text{O})-\text{alkyl}$ ,  $-\text{O}-\text{CH}_2-\text{CH}(\text{O}-\text{C}(\text{O})-\text{R}_6)-\text{CH}_2(\text{O}-\text{C}(\text{O})-\text{R}_7)$ ,  $-\text{O}-\text{CH}_2-\text{CH}(\text{OR}_6)-\text{CH}_2(\text{OR}_7)$ ,  $-\text{O}-\text{CH}_2-\text{CH}(\text{R}_6)-\text{CH}_2(\text{R}_7)$ ,  $-\text{O}-(\text{CH}_2)_m-\text{cholesterol}$ , polyethylene glycol,  $-\text{O}-(\text{CH}_2)_n-\text{N}^+(\text{R}_8)_3$ ,  $-\text{NH}_2$ ,  $-\text{N}^+(\text{CH}_3)_3$ ,  $-(\text{CH}_2)_n-\text{N}^+(\text{R}_9)_3$ ,  $-(\text{CH}_2)-\text{OR}_{10}$  where  $\text{R}_6$ ,  $\text{R}_7$ ,  $\text{R}_8$ ,  $\text{R}_9$ , and  $\text{R}_{10}$  are independently selected from the group consisting of hydrogen, methyl, and alkyl, and where  $m$  is selected from the group consisting of 0, 1, 2, 3, 4, and 5, and where  $n$  is selected from the group consisting of 1, 2, 3, 4, and 5.

2) Please delete the ~~second~~ <sup>third</sup> full paragraph on page ~~8~~ <sup>9</sup>, starting from line 8 and ending with line ~~18~~ <sup>10</sup> of page ~~9~~ <sup>10</sup> with the following replacement paragraph:

In another aspect, the invention features a compound having a structure set forth in formula I:



(I)

where (a)  $\text{R}_1$  and  $\text{R}_{1'}$  are independently selected from the group consisting of hydrogen,  $-\text{OH}$ ,  $-\text{OCH}_3$ ,  $-\text{alkyl}$ ,  $-\text{O}-\text{alkyl}$ ,  $-\text{O}-\text{C}(\text{O})-\text{alkyl}$ ,  $-\text{O}-\text{CH}_2-\text{CH}(\text{O}-\text{C}(\text{O})-\text{R}_6)-\text{CH}_2(\text{O}-\text{C}(\text{O})-\text{R}_7)$ ,  $-\text{O}-\text{CH}_2-\text{CH}(\text{OR}_6)-\text{CH}_2(\text{OR}_7)$ ,  $-\text{O}-\text{CH}_2-\text{CH}(\text{R}_6)-\text{CH}_2(\text{R}_7)$ ,  $-\text{O}-(\text{CH}_2)_m-\text{cholesterol}$ , polyethylene glycol,  $-\text{O}-(\text{CH}_2)_n-\text{N}^+(\text{R}_8)_3$ ,  $-\text{NH}_2$ ,  $-\text{N}^+(\text{CH}_3)_3$ , and  $-(\text{CH}_2)_n-\text{N}^+(\text{R}_9)_3$ , where  $\text{R}_6$ ,  $\text{R}_7$ ,  $\text{R}_8$ , and  $\text{R}_9$  are independently selected from the group consisting of hydrogen, methyl, and alkyl, and where  $m$  is selected from the group consisting of 0, 1, 2, 3, 4, and 5, and where  $n$  is selected from the group consisting of 1, 2, 3, 4, and 5; (b)  $\text{R}_2$  and  $\text{R}_{2'}$  are independently selected from the group consisting  $-\text{NH}_2$ ,  $-\text{N}^+(\text{CH}_3)_3$ ,

$-(CH_2)_n-N^+(R_{11})_3$ , and  $-NH-C(N^+H_2)-NH_2$ , wherein  $R_{11}$  is selected from the group consisting of hydrogen, methyl, and alkyl; and (c)  $R_3, R_3', R_4, R_4', R_5$ , and  $R_5'$  are independently selected from the group consisting of hydrogen,  $-OH$ ,  $-OCH_3$ ,  $-alkyl$ ,  $-O-alkyl$ ,  $-O-C(O)-alkyl$ ,  $-O-CH_2-CH(O-C(O)-R_6)-CH_2(O-C(O)-R_7)$ ,  $-O-CH_2-CH(OR_6)-CH_2(OR_7)$ ,  $-O-CH_2-CH(R_6)-CH_2(R_7)$ ,  $-O-(CH_2)_m$ -cholesterol, polyethylene glycol,  $-O-(CH_2)_n-N^+(R_8)_3$ ,  $-NH_2$ ,  $-N^+(CH_3)_3$ , and  $-(CH_2)_n-N^+(R_9)_3$ , where  $R_6, R_7, R_8$ , and  $R_9$ , are independently selected from the group consisting of hydrogen, methyl, and alkyl, and where  $m$  is selected from the group consisting of 0, 1, 2, 3, 4, and 5, and where  $n$  is selected from the group consisting of 1, 2, 3, 4, and 5, provided that  $R_5'$  is not  $-CH_2-O-C(O)-(CH_2)_{14}CH_3$  when  $R_3'$  and  $R_4'$  are  $-OH$  and  $R_2'$  is  $-NH_2$  and  $R_1'$  is  $-OCH_3$ , and provided that  $R_5'$  is not  $-CH_2-O-C(O)-(CH_2)_pCH_3$ , where  $p$  is selected from the group consisting of 10, 12, 14, or 16, when  $R_3'$  is identical to  $R_5'$  and  $R_4'$  is  $-OH$  and  $R_2'$  is  $-NH_2$  and  $R_1'$  is  $-OCH_3$ .

3) Please delete the <sup>second</sup> ~~fourth~~ full paragraph on page <sup>14</sup> ~~12~~, starting from line <sup>8</sup> ~~21~~ and ending with line <sup>18</sup> ~~30~~ with the following replacement paragraph:

In yet another preferred embodiment, the invention relates to the compound of formula (I), where  $R_1$  and  $R_1'$  are independently selected from the group consisting of hydrogen,  $-OCH_3$ ,  $-alkyl$ ,  $-O-alkyl$ ,  $-O-C(O)-alkyl$ ,  $-O-CH_2-CH(alkyl)-CH_2(alkyl)$ ,  $-O-CH_2-CH(O-alkyl)-CH_2(O-alkyl)$ ,  $-O-CH_2-CH(O-C(O)-alkyl)-CH_2(O-C(O)-alkyl)$ ,  $-O-(CH_2)_m$ -cholesterol, polyethylene glycol,  $-O-(CH_2)_n-NH_2$ , and  $-O-(CH_2)_n-N^+(CH_3)_3$ , where  $m$  is selected from the group consisting of 0, 1, 2, 3, 4, and 5, and where  $n$  is selected from the group consisting of 1, 2, 3, 4, and 5.

- 4) Please delete the <sup>second</sup> ~~third~~ full paragraph on page <sup>18</sup> ~~16~~, starting from line 16 and ending with page <sup>17</sup> ~~17~~, line <sup>9</sup> ~~5~~, with the following replacement paragraph:

Thus in another aspect, the invention features a compound for delivering one or more macromolecules into cells, comprising: (a) a compound comprising a glycosyl moiety having a nitrogen-based substituent linked to a carbon atom within the glycosyl moiety, where the nitrogen-based substituent is selected from the group consisting of  $-\text{NH}_2$ ,  $-\text{N}^+(\text{CH}_3)_3$ ,  $-(\text{CH}_2)_n-\text{N}^+(\text{R}_{10})_3$ , and  $-\text{NH}-\text{C}(\text{N}^+\text{H}_2)-\text{NH}_2$ , and where substituents linked to other carbon atoms within the glycosyl moiety are selected from the group consisting of hydrogen, -alkyl, -O-alkyl,  $-\text{O}-\text{C}(\text{O})-\text{alkyl}$ ,  $-\text{O}-\text{CH}_2-\text{CH}(\text{O}-\text{C}(\text{O})-\text{R}_6)-\text{CH}_2(\text{O}-\text{C}(\text{O})-\text{R}_7)$ ,  $-\text{O}-\text{CH}_2-\text{CH}(\text{OR}_6)-\text{CH}_2(\text{OR}_7)$ ,  $-\text{O}-\text{CH}_2-\text{CH}(\text{R}_6)-\text{CH}_2(\text{R}_7)$ ,  $-\text{O}-(\text{CH}_2)_m$ -cholesterol, polyethylene glycol,  $-\text{O}-(\text{CH}_2)_n-\text{N}^+(\text{R}_8)_3$ ,  $-\text{NH}_2$ ,  $-\text{N}^+(\text{CH}_3)_3$ ,  $-(\text{CH}_2)_n-\text{N}^+(\text{R}_9)_3$ ,  $-(\text{CH}_2)-\text{OR}_{10}$  where  $\text{R}_6$ ,  $\text{R}_7$ ,  $\text{R}_8$ ,  $\text{R}_9$ , and  $\text{R}_{10}$  are independently selected from the group consisting of hydrogen, methyl, and alkyl, and where  $m$  is selected from the group consisting of 0, 1, 2, 3, 4, and 5, and where  $n$  is selected from the group consisting of 1, 2, 3, 4, and 5; and (b) the macromolecule or macromolecules.

- 5) Please delete the first full paragraph on page <sup>19</sup> ~~17~~, starting from line <sup>10</sup> ~~6~~ and ending with line <sup>9</sup> ~~33~~ with the following replacement paragraph:

In another aspect, the invention features a composition for delivering one or more macromolecules into cells, comprising: (a) a compound having a structure set forth in formula (I), where (i)  $\text{R}_1$  and  $\text{R}_1'$  are independently selected from the group consisting of hydrogen,  $-\text{OH}$ ,  $-\text{OCH}_3$ , -alkyl, -O-alkyl,  $-\text{O}-\text{C}(\text{O})-\text{alkyl}$ ,  $-\text{O}-\text{CH}_2-\text{CH}(\text{O}-\text{C}(\text{O})-\text{R}_6)-\text{CH}_2(\text{O}-\text{C}(\text{O})-\text{R}_7)$ ,  $-\text{O}-\text{CH}_2-\text{CH}(\text{OR}_6)-\text{CH}_2(\text{OR}_7)$ ,  $-\text{O}-\text{CH}_2-\text{CH}(\text{R}_6)-\text{CH}_2(\text{R}_7)$ ,  $-\text{O}-(\text{CH}_2)_m$ -cholesterol,  $-\text{O}-(\text{CH}_2)_n-\text{N}^+(\text{R}_8)_3$ ,  $-\text{NH}_2$ ,  $-\text{N}^+(\text{CH}_3)_3$ ,  $-(\text{CH}_2)-\text{N}^+(\text{R}_9)_3$ , and  $-(\text{CH}_2)-\text{OR}_{10}$ , where  $\text{R}_6$ ,  $\text{R}_7$ ,  $\text{R}_8$ ,  $\text{R}_9$ , and  $\text{R}_{10}$  are independently selected from the group consisting of hydrogen, methyl, and alkyl, and

where m is selected from the group consisting of 0, 1, 2, 3, 4, and 5, and where n is selected from the group consisting of 1, 2, 3, 4, and 5; (ii)  $R_2$  and  $R_2'$  are independently selected from the group consisting of hydrogen,  $-\text{NH}_2$ ,  $-\text{N}^+(\text{CH}_3)_3$ ,  $-(\text{CH}_2)_n-\text{N}^+(\text{R}_{10})_3$ , and  $-\text{NH}-\text{C}(\text{N}^+\text{H}_2)-\text{NH}_2$ , wherein  $\text{R}_{10}$  is selected from the group consisting of hydrogen, methyl, and alkyl; and (iii)  $R_3$ ,  $R_3$ ,  $R_4$ ,  $R_4'$ ,  $R_5$ , and  $R_5'$  are independently selected from the group consisting of hydrogen,  $-\text{OH}$ ,  $-\text{OCH}_3$ ,  $-\text{alkyl}$ ,  $-\text{O-alkyl}$ ,  $-\text{O-C(O)-alkyl}$ ,  $-\text{O-CH}_2-\text{CH}(\text{O-C(O)-R}_6)-\text{CH}_2(\text{O-C(O)-R}_7)$ ,  $-\text{O-CH}_2-\text{CH}(\text{OR}_6)-\text{CH}_2(\text{OR}_7)$ ,  $-\text{O-CH}_2-\text{CH}(\text{R}_6)-\text{CH}_2(\text{R}_7)$ ,  $-\text{O-(CH}_2)_m\text{-cholesterol}$ ,  $-\text{O-(CH}_2)_n-\text{N}^+(\text{R}_8)_3$ ,  $-\text{NH}_2$ ,  $-\text{N}^+(\text{CH}_3)_3$ ,  $-(\text{CH}_2)_n-\text{N}^+(\text{R}_9)_3$ , and  $-(\text{CH}_2)-\text{OR}_{10}$ , where  $\text{R}_6$ ,  $\text{R}_7$ ,  $\text{R}_8$ ,  $\text{R}_9$ , and  $\text{R}_{10}$  are independently selected from the group consisting of hydrogen, methyl, and alkyl, and where m is selected from the group consisting of 0, 1, 2, 3, 4, and 5, and where n is selected from the group consisting of 1, 2, 3, 4, and 5; and (b) the macromolecule or macromolecules.

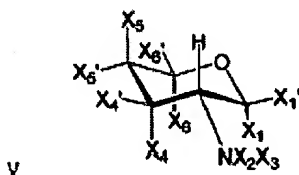
- 6) Please delete the <sup>5th</sup> full paragraph on page <sup>22</sup>20, starting from line <sup>29</sup>12 and ending with line <sup>11</sup>24 on page <sup>23</sup>23 with the following replacement paragraph:

In yet another preferred embodiment, the invention relates to the composition, where  $\text{R}_1$  and  $\text{R}_1'$  are independently selected from the group consisting of  $-\text{OCH}_3$ ,  $-\text{alkyl}$ ,  $-\text{O-alkyl}$ ,  $-\text{O-C(O)-alkyl}$ ,  $-\text{O-CH}_2-\text{CH}(\text{alkyl})-\text{CH}_2(\text{alkyl})$ ,  $-\text{O-CH}_2-\text{CH}(\text{O-alkyl})-\text{CH}_2(\text{O-alkyl})$ ,  $-\text{O-CH}_2-\text{CH}(\text{O-C(O)-alkyl})-\text{CH}_2(\text{O-C(O)-alkyl})$ ,  $-\text{O-(CH}_2)_m\text{-cholesterol}$ ,  $-\text{O-(CH}_2)_n-\text{NH}_2$ , and  $-\text{O-(CH}_2)_n-\text{N}^+(\text{CH}_3)_3$ , where m is selected from the group consisting of 0, 1, 2, 3, 4, and 5, and where n is selected from the group consisting of 1, 2, 3, 4, and 5. In other preferred embodiments, the invention relates to the composition, where the alkyl moiety is a straight chain hydrocarbon moiety having 14, 16, or 18 carbon atoms and 0, 1, 2, or 3 unsaturations.

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7) Please delete the ~~third~~ full paragraph on page ~~28~~, starting from line ~~12~~ and ending with page ~~29~~, line ~~6~~ with the following replacement paragraph:

In yet another aspect, the invention features a method for synthesizing a compound of the invention, comprising the steps of: (a) reacting a first reactant of formula (V):



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With a second reactant, where  $X_1$  and  $X_1'$  are independently selected from the group consisting of hydrogen, halogen atom, and an activatable moiety;  $X_2$  and  $X_3$  are independently selected from the group consisting of a protecting moiety, hydrogen, halogen, or any activatable moiety; and where  $X_4$ ,  $X_4'$ ,  $X_5$ ,  $X_5'$ ,  $X_6$ , and  $X_6'$  are independently selected from the group consisting of hydrogen,  $-O$ -acetyl,  $-OH$ ,  $-CH_2-O$ -acetyl,  $-CH_2-OH$ , and  $-O$ -alkyl; where the second reactant is selected from the group consisting of  $HOCH_3$ ,  $HO$ -alkyl,  $HO-C(O)$ -alkyl,  $HO-CH_2-CH(O-C(O)-R_6)-CH_2(O-C(O)-R_7)$ ,  $HO-CH_2-CH(OR_6)-CH_2(OR_7)$ ,  $HO-CH_2-CH(R_6)-CH_2(R_7)$ ,  $HO-(CH_2)_m$ -cholesterol,  $HO-(CH_2)_n-N(R_8)_3$ , where  $R_6$ ,  $R_7$ , and  $R_8$  are independently selected from the group consisting of hydrogen, methyl, and alkyl, and where  $m$  is selected from the group consisting of 0, 1, 2, 3, 4, and 5, and where  $n$  is selected from the group consisting of 1, 2, 3, 4, and 5; (b) reacting the product of step (a) with a reducing agent; and (c) purifying the compound of the invention.